Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

STRESS, GUT HEALTH AND ACNE: EXPLORING PSYCHO-INTESTINAL LINKS IN ACNE PATHOGENESIS

Ayet ul Haya
Student of dermatology technology. (Semester 8), Department of Emerging Allied Health Technologies, Faculty of Allied Health Sciences. University of Lahore
Email ayatulhaya6@gmail.com
Dr. Saima Saif *
Senior Demonstrator, Department of Emerging Allied Health Technologies. Faculty of Allied Health Sciences. University of Lahore
Email saima.saif@ahs.uol.edu.pk

Author Details

Keywords:
Stress, acne vulgaris, gut health, gut-brain-skin axis, gut-skin axis, dysbiosis

Received on 24 March, 2026
Accepted on 24 April, 2026
Published on 08 May, 2026

Corresponding E-mails & Authors*:
Dr. Saima Saif

Abstract

Acne vulgaris is a commonly occurring inflammatory skin disorder that affects both adults and teenagers and often causes considerable psychological distress. By emphasising the psycho-intestinal pathways that link stress, gut microbiota, and skin inflammation, this narrative review aimed to evaluate the role of psychological stress and gut health on the development of acne. In order to investigate the relationships between stress, dietary impacts, microbial imbalances, and the beginning of acne, evidence from international studies published over the past 20 years is examined. These studies include clinical, epidemiological, and mechanistic investigations. Based on the findings, a complicated interplay between follicular hyper keratinization, increased sebum production, microbial presence, and localized inflammation causes acne. The hypothalamic-pituitary-adrenal axis becomes active by psychological stress, resulting in elevated cortisol and neuropeptide levels that

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

stimulate inflammatory responses and improve sebaceous gland activity. The gut–brain–skin axis plays an important role in the development of disease because dysbiosis of the gut microbiota simultaneously causes oxidative stress, impaired skin barrier integrity, and systemic immunological dysfunction. While nutrients including antioxidants, polyphenols, omega-3 fatty acids, and probiotics demonstrate protective effects by reducing inflammation and improving microbial balance, eating habits characterized by high glycaemic load and excessive dairy consumption may exacerbate hormonal and metabolic problems. Clinical outcomes and patient quality of life may be improved by combining standard dermatological treatments with stress management strategies, dietary modifications, and microbiome-focused therapy. To improve acne treatment and efficacy, future research should focus on customised approaches that consider microbial, nutritional, and psychological factors.

INTRODUCTION

Acne vulgaris is one of the leading inflammatory skin disorders common in approximately 85% of the adolescent group as well as a significant percentage of adults around the world (1,2).It appears as a group of comedones , papules, pustules, nodules, as well as cysts predominantly on the chest, back, as well as the face. Acne considerably impacts psychological health with a typical outcome being lowered self-esteem, social avoidance, as well as depression, anxiety (3–5). In the traditional mind-set, acne pathogenesis was blamed primarily on follicular hyper keratinization, increased sebum secretion, microbial colonization by Cuti bacterium acnes, as well as localized inflammation (1,5,6). However, systemic factors such as the intestinal microbiome as well as psychological pressure significant in the regulation of disease onset as well as severity (1,2,6,7).

The hypothalamic-pituitary-adrenal (HPA) axis, a major neuroendocrine system that controls the body's reaction to stress by regulating interactions between the hypothalamus, pituitary gland, and adrenal cortex, is activated by stress, which accelerates acne. It works by releasing

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

corticotropin-releasing hormone from the brain, which stimulates the pituitary gland to release adrenocorticotropic hormone, which causes the adrenal glands to release cortisol (3,7–9). The dysbiosis in gut can impinge on systemic immunity, oxidative stress, and metabolic activity, thus contributing indirectly to skin health as well as acne intensity (2–4,10). These pathways do not operate in a vacuum but converge over the gut-brain-skin axis, such that stress-induced changes in the composition of the gut microbiome could exacerbate systemic inflammation as well as acne advancement (2,11–13).

Acne Pathophysiology and Skin Microbiome Acne is caused by a complicated interplay between skin-related variables, microorganisms, bodily systems, and the immune response(1,2,7,11). Cutibacterium acnes plays a central role not only because of its hyperproliferation but also because of the dysbiosis noted in its phylotypes, predominantly IA1, that triggers innate auto-inflammatory activation as well as cutaneous inflammation enhancement (1,7). The skin homeostasis disruption further exacerbates the imbalance between C. acnes phylotypes versus other commensal bacteria like Staphylococcus epidermidis leading to enhanced release of pro-inflammatory cytokines as well as keratinocyte dysfunction (1,4).

Acne is more than a localized skin disease involving systemic immunometabolism dysregulation (1,2,7). Reactive oxygen species (ROS) produced in sebaceous glands can reinforce inflammation, for instance, whereas hormonal factors such as androgens and insulin-like growth factor-1 (IGF-1) upregulate sebum synthesis and change follicular keratinization (7,11,14). More lifestyle factors such as diet, sleep, and stress regulate these pathways further impacting acne severity (1,7,12).For example, Dietary-high-glycaemic index meals could potentially exacerbate insulin as well as IGF-1 signalling to promote sebaceous gland hyperactivity, whereas stress-induced cortisol release will increase sebocyte cell division as well as inflammatory mediator synthesis (3,4,7,8).

The interventions aimed at the skin microbiome, including topical probiotics or skincare products designed to be microbiome-friendly, may mitigate inflammatory lesions by reinstating

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

microbial equilibrium without disrupting commensal strains (1,7,14). The systemic alterations of the gut microbiome through the use of probiotics, prebiotics, or dietary modifications can affect skin inflammation via the gut-skin axis, thereby illustrating a connection between microbial metabolites, immune regulation, and dermal health(2,4,11–13).

Stress and Acne

It is known that psychological stress has a significant role in aggravating acne by activating the hypothalamic-pituitary-adrenal (HPA) axis, which raises cortisol and neuropeptide release. These neuroendocrine alterations increase the activity of sebaceous glands and encourage the of inflammatory mediators linked to the aetiology of acne (3,6,15,16). Acne severity has been linked to both acute and chronic stress, especially in young adults and adolescents, where higher perceived stress levels are linked to more severe acne (16,12,8). Independent of other contributing factors like sleep and food habits, situational stress, such as academic pressure, has also been connected to a markedly elevated risk of acne(6). Figure 1 outlines the mechanism pathway relating stress as a cause of cutaneous immunologic responses as well as barrier disruption.(9)

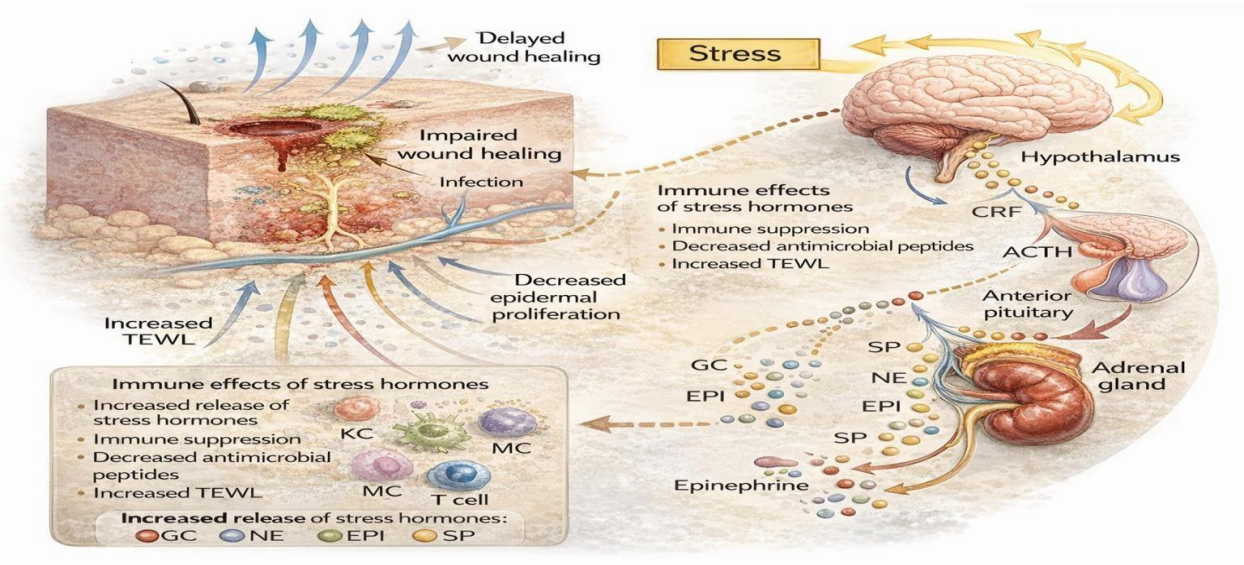

Figure 1 stress induced effects on skin barrier:

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

Stress activates the amygdala, leading to CRF release, which stimulates the anterior pituitary to secrete ACTH. This triggers adrenal gland production of glucocorticoids (GC) and epinephrine (EPI), while nerve signals release substance P (SP) and noradrenaline (NE). These neuroendocrine factors interact with skin cells—including keratinocytes (KC), dendritic cells (DC), mast cells (MC), and T cells—promoting inflammatory cytokines (IL-1, IL-4, IL-5, IL-6, IL-18, TNF), reducing antimicrobial peptides, increasing transepidermal water loss (TEWL), and delaying wound healing, collectively impairing skin barrier function.

Stress always comes out as one of the key aggravating factors in the pathophysiology of acne. There are several observational and experimental studies that verify that increased levels of stress are associated with more severe acne, particularly among adolescents and young adults (3,8,10,13,17–19). Stress hormones such as cortisol and catecholamines stimulate sebaceous glands, enhance lipogenesis, and enhance inflammatory signals (3,14,20). Specifically, Substance P has been demonstrated to stimulate sebocyte proliferation and cytokine secretion, feeding back onto inflammatory cascades (21). Clinically, these mechanistic observations are mirrored: patients with elevated academic or psychosocial stress manifest more inflammatory lesions, and longitudinal studies show deterioration during exam times (13,17–19). However, there is heterogeneity some groups have weaker correlations, which indicates that host genetics or microbiome abundance might mediate between-group differences (9,15,22). Notably, the psychologic impact of acne itself reinforces this vicious cycle; visible lesions stoke fear, depression, and withdrawal from social interactions (13,15,22,23), which reciprocally increase stress responses and perpetuate flare-ups. Together, these results are consistent with a reciprocal stress–acne interaction operating at a level deeper than skin.

Gut Microbiome and Acne

Dysbiosis, or changes in the composition of the gut microbiota, has been linked to the pathophysiology of acne through its impact on neuroendocrine control, inflammatory signalling, and systemic immunity (2,4,7,11,13). Individuals with acne have been shown to exhibit

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

imbalances in gut microbial populations, including reduced beneficial bacteria and altered microbial diversity (13). Bidirectional communication routes connect the gut and skin, and microbial metabolites including secondary bile acids and short-chain fatty acids help control cutaneous and systemic inflammation (2).

One potential mechanism is the interaction with the mTOR (mammalian target of rapamycin) pathway as a possible influence of the gut microbiota in acne. In fact, several skin diseases have been found to have a deregulated mTOR pathway recently. In the skin, in general, mTOR is a nutrient-sensitive regulator involved in processes of cell growth and differentiation, being key in maintaining homeostasis, and at building an adequate epidermal barrier. Mistakes in the mTOR pathway negatively affect these processes in different skin diseases. Monfrecola et al. have been able to prove for the first time the role of mTOR in acne pathogenesis, finding an increase in the expression of mTOR in acne patients in both affected and healthy skin of mTOR compared to healthy controls. Likewise, studies in mice have shown that by causing glucose intolerance and obesity through a diet with a high glycemic load that modified mTOR activity, it was related to specific changes in composition of gut microbiota that were evidenced inversely by administering resveratrol (specific inhibitor of mTOR complex 1) to these mice. These studies linked to the effects of diet, intestinal microbiota, and pathogenesis of acne related to the mTOR pathway. Moreover, the metabolites produced by bacteria can play a role in the mTOR pathway and the mTOR pathway can modulate the gut microbiota by regulating the intestinal barrier.

Thus, creating an altered intestinal barrier in an intestinal dysbiotic environment can positive feedback loop that can exacerbate inflammation and worsen acne.

Combined Stress–Gut–Acne Interactions

Stress-induced activation of the HPA axis in conjunction with gut dysbiosis can intensify systemic inflammatory reactions and exacerbate acne lesions (6). Psychological stress may change intestinal function and the makeup of gut microbes, increasing inflammation that impacts skin health. The gut–brain–skin axis, which explains the intricate interplay between the

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

gastrointestinal, dermatological, and psychological systems, explains this interaction (2,7,11,22,25). Therefore, compared to single-modality therapies, a holistic therapeutic approach that incorporates stress management, dietary modifications, probiotic supplements, and traditional pharmaceutical treatment may yield better results (1,2,11,12,15). A combinational approach can influence several pathways concomitantly, such as by modulating the immune system, neuroendocrine system regulation, and microbiome equilibrium, enhancing clinical responses as well as quality of life in patients.

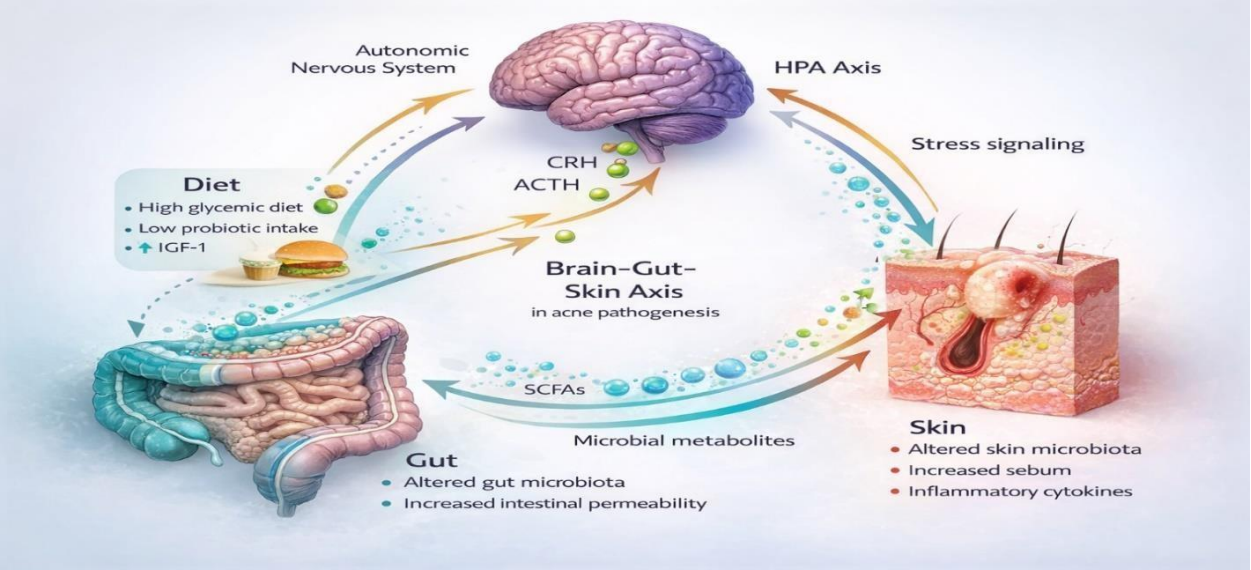

Figure 2: Schematic representation of the psycho–intestinal–cutaneous axis. Stress and dietary factors alter gut microbiota and impair the gut barrier, leading to systemic inflammation and metabolite entry into the bloodstream. These changes affect skin homeostasis through the skin HPA axis and autonomic nervous system, contributing to acne development. Gut microbiota also modulates immunity and directly influences skin function via short-chain fatty acids (SCFAs).

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

METHODOLOGY

By methodically searching PubMed, Scopus, Web of Science, and Google Scholar for articles published between 2000 and 2025 using phrases such "acne vulgaris," "stress," "gut microbiome," "diet," and "gut–brain–skin axis," this narrative review focused on the relationship between stress, gut health, and acne. Clinical trials, observational studies, and systematic or high-quality narrative reviews that examined the pathophysiology of acne in connection to psychological stress, gut microbial dysbiosis, or dietary variables were all considered eligible studies. Following the screening of more than 300 records, 51 relevant publications were chosen and evaluated by a thematic analysis in order to highlight inconsistencies, identify gaps in the psycho-intestinal model of acne, and summarize convergent evidence.

DISCUSSION

The interaction between stress, intestinal health, and acne has long intrigued scientists, as far back as the beginning of the 20th century when Stokes and Pillsbury first postulated that psychogenic distress might cause intestinal dysfunction that systemically exacerbates acne symptoms (26). Their idea was resuscitated and up-to-date by Bowe and Logan, who provide evidence that imbalances in the gut microbial community exert effects on oxidative stress, glucose homeostasis, and immunity that underlie the gut–skin axis as a biologically realistic contributor to acne vulgaris (25,26). Microbiota-focused investigation further highlights the association between intestinal health and cutaneous disease. Sánchez-Pellicer et al. demonstrate that intestinal and cutaneous microbial imbalances cross over between hormonal and hereditary determinants of acne risk such that probiotics might inhibit burning, restore intestinal integrity, and normalize IGF-1 pathway signalling, although firm clinical confirmation still remains lacking(27). This microbiome-centred paradigm was repeated by Lee et al., who contended that the severity of acne might not merely be a product of C. acnes burden but instead reflects distinctions in virulent clades such that stress

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

and intestinal dysbiosis might be part of a gut–brain–skin network interacting with this severity (18). Latest breakthroughs employing Mendelian randomization further solidify these relationships: Cao et al. implicate taxa such as Allisonella and Bacteroides as promising microbial determinants of risk such that He et al. as well as Ji et al. show that metabolites such as DHA as well as protective taxa such as Lactobacillus might mediate acne outcomes (28–30). Even more recently, Salem et al. as well as Sánchez-López et al. reaffirmed the idea that pre-existing disruptions in microbiota frequently antedate the development of skin inflammatory disorders such that oral as well as topically administered probiotics rise as promising adjunct strategies (2,31). Huang et al. further highlight the importance of gut-derived tryptophan metabolites in establishing a link between microbial metabolism and immunological and neuroendocrine system modulation (32). The skin is an important sign of gut health since microbial dysbiosis is linked to acne, psoriasis, rosacea, and systemic inflammatory diseases, according to more thorough mechanistic investigations like those presented by Pai et al. and Mahmud et al (14,33). Oxidative stress is a significant pathway of acne pathogenesis in addition to microbiological causes. According to Arican et al., people with acne have very dysregulated levels of antioxidant enzymes, with elevated levels of superoxide dismutase and malondialdehyde and decreased levels of catalase and glucose-6-phosphate dehydrogenase, indicating a disruption of redox homeostasis (4). Ni et al. elaborate on the finding by explaining how oxidative stress is increased by gut dysbiosis, leading to systemic inflammation that exacerbates dermatological outcomes (34). Bungau et al. connected these results to metabolic disruption, suggesting that acne and obesity and insulin resistance share pathophysiologic pathways and recommending dietary antioxidants and phytochemicals as treatment possibilities (35). Baldwin and Tan further illustrate how dietary modifications, such as low-glycaemic meals and omega-3 fatty acids, might limit the severity of acne by highlighting the influence of nutrition on oxidative and inflammatory control (36). All of these results point to the confluence of oxidative stress, microbial imbalance, and systemic metabolic regulation in acne aetiology (4,36–38). Alzahrani et al. once more verified in a

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

systematic review that stress was substantially linked to the severity of acne among Middle Eastern medical students, providing new evidence for this association (39), with Basfar et al. found that stress and poor diets are linked to more severe acne in Saudi students (40). Beyond the field of dermatology, Nagamine shows how the gut-skin-brain axis in systemic disease interacts with stress and psychological symptoms including anxiety and sleep

disorders (41), with Maiuolo et al. associating microbiota dysbiosis with stress-mediated neurological disorders, indirectly supporting its role in skin inflammation (42). When taken as a whole, these findings highlight how stress can aggravate acne through neuroimmune, metabolic, and microbiological processes in addition to acting as an underlying cause (36,39–43).

Research on acne has consistently focused on the effect of stress, which is backed by both clinical and experimental findings. Regardless of any quantifiable changes in sebum secretion, Yosipovitch and colleagues show in teenagers that perceived stress corresponds with illness severity, indicating that immune system or barrier-mediated processes rather than sebaceous function in and of itself are more important (20). According to Jusuf et al., acne patients elevated serum levels of substance P, a neuropeptide released in response to stress, were linked to higher stress scores and may have a pro-inflammatory effect on sebaceous gland output (20,44). The relationship between psychological stress and microbiological toxicity is further clarified by Borrel et al., who demonstrate that catecholamines directly influence C. acnes to enhance biofilm formation and sebocyte lipid synthesis (45). According to Zhang et al., these results fit into a neuroendocrine-immune paradigm in which stress triggers the hypothalamic-pituitary-adrenal axis, which in turn causes cytokine dysregulation and disruption of the skin barrier, aggravating acne symptoms (46). Additionally, Gradowicz-Prajsnar explains the vicious loop in which excess cortisol from prolonged stress weakens skin pathogenesis and interacts with microbial and neuroimmune systems (47). When taken as a whole, these research highlight the fact that stress both causes and exacerbates acne (20,44–47). These mechanistic discoveries have been reinforced by further evidence from clinical and epidemiological research. Aziz and Khan, in their cross-sectional study among medical

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

students, demonstrate a very significant correlation of positive degree between severity of acne and academic stress, with examination being a key stimulus(19). Sutrisno and Jusuf also demonstrate this, observing an association between higher stress scores and greater severity of acne among young adults (44). Zari and Alrahmani replicate these results in female medical students, and they showed that higher perceived stress scores were related to more severe acne after adjusting for confounders(3). Bouraqqadi et al. replicates these trends in Moroccan medical students, and they found higher acne severity during times of high stress when compared to baseline (6). In contrast, however, one study conducted at YARSI University failed to identify a statistically significant link between stress and acne, and it was speculated that the interaction between stress and acne may vary in populations by cultural, genetic, or lifestyle background (48). Overall, however, most studies reflect a consistent aggravating impact of psychological stress on the severity of acne (3,6,19,44,48).

New gut microbiota research provides compelling evidence that acne is not only a cutaneous disease but also an expression of systemic disbalances in different organ systems. Salem et al. argues that imbalance in the microbial communities of the gut damages immune tolerance and supports chronic low-grade inflammation, which manifests on the skin as acne and other dermatoses(2). Bowe and Logan had earlier hypothesized that probiotics such as Lactobacillus and Bifidobacterium produce short-chain fatty acids, reduce oxidative stress, and alter glycaemic control, potentially rendering dietary modulation of microbiota an adjunct to conventional acne treatment (25). More recently, Chilicka et al. demonstrates that probiotic supplementation can alter sebum composition and inflammatory markers, highlighting a possible translational pathway for gut-focused therapies in dermatology (49). Collectively, these studies suggest that therapy guided by microbiota can offer valuable adjuncts to standard pharmacologic therapy (2,25,49).

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

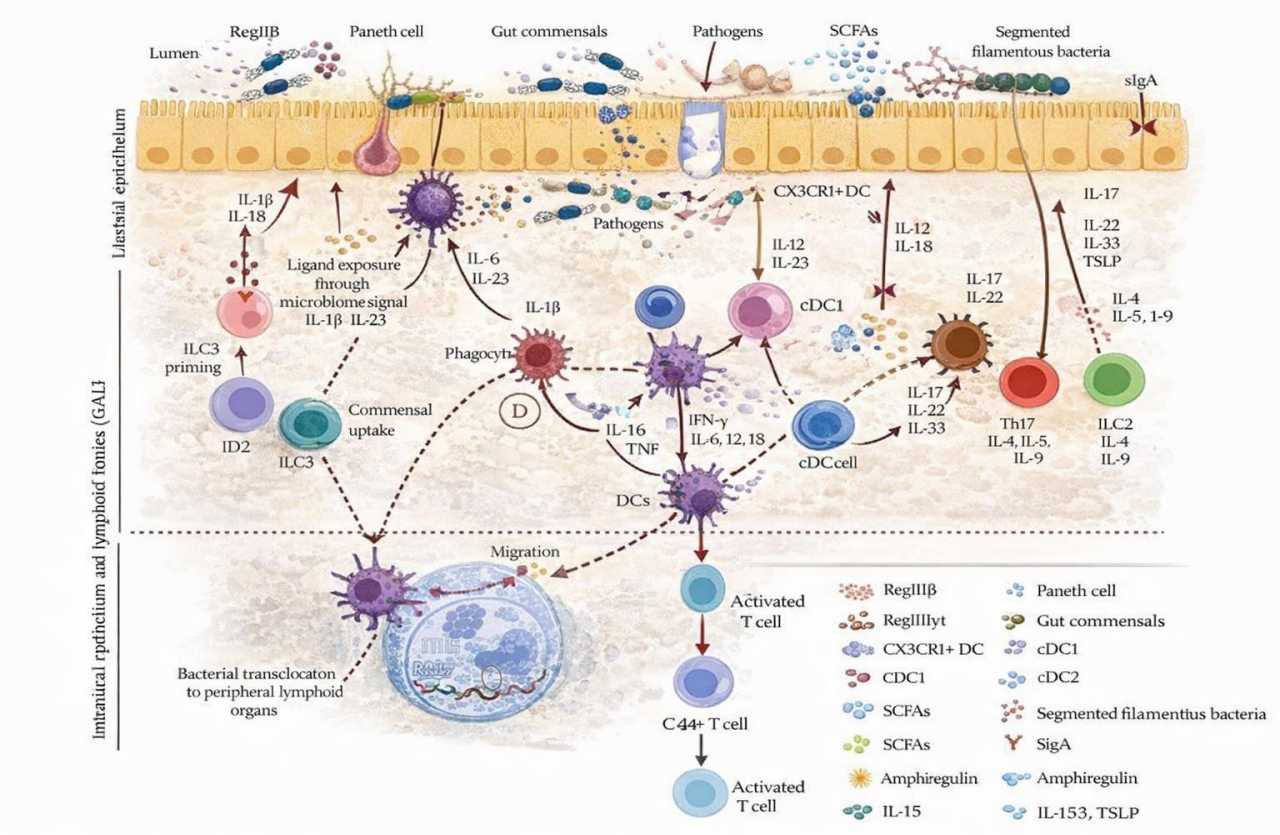

Figure 3 Gut–Skin Immuno-Crosstalk:

This figure illustrates immune interactions between the gut and skin. (A) CX3CR1+ DCs phagocytose antigens, while CD103+ DCs migrate to Peyer's patches or mesenteric lymph nodes to activate naive T cells. Activated DCs release IL-12, IL-15, and IFNs to stimulate cNK cells. (B) SCFAs enhance DC cytokine production (IL-6, IL-12, IFN, TNF), further training cNK cells. (C–D) MAIT cells are activated by IL-12, IL-15, IL-18, and TNF-like proteins, while phagocytes secrete IL-6 and IL-23. (E) Foxp3+ Tregs and Tfh/ex-Th17 cells in Peyer's patches promote B cell class switching and sIgA production, maintaining microbiome homeostasis. (F–H) ILC2 and ILC3 respond to epithelial cytokines and microbial signals, with ILC3 secreting IL-22 to induce antimicrobial peptides (REGIIIβ, REGIIIγ) and support pathogen defense. Adapted from references 55–58; created with BioRender.com (2022).

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

Nutritional influences overlap with microbiome and stress pathways in the formation of acne and different studies have reported that consumption of nutrients controls microbial diversity, immune signalling, and cutaneous inflammation(7,49). Li et al. reports that dietary polyphenols, probiotics, and gut-metabolized food nutrients reduce systemic inflammation and improve skin barrier function, which is a potential for diet control of acne (7). Chilicka et al. also supports the application of probiotics, with their ability to normalize intestinal and skin microbiota balance, therefore reducing lesion formation(49). Baldwin and Tan validate that omega-3 fatty acids antioxidants such as vitamin D and polyphenols possess anti-inflammatory actions on acne, at least partially, by cytokine modulation and reactive oxygen species (36). In addition, He et al. shows through Mendelian randomization that gut microbial metabolites significantly influence acne risk, and Sivamani et al. highlights correlations between gut microbial diversity, androgenic hormone levels, and severity of acne (29,50). Collectively, these findings suggest an integrated dietary–microbial–immunological model of acne in which diet not only triggers metabolic and hormonal changes but also dictates microbiota-mediated inflammation(7,29,36,49,50). Jusuf et al. highlights that hormonal changes caused by stress, including elevations in cortisol and androgens, directly exacerbate the activity of sebaceous glands and inflammation, thereby exacerbating the severity of acne(44). Zhang et al. also provides evidence that stress affects immune and microbial mechanisms, promoting cutaneous inflammation through gut–brain–skin interactions (46). Borrel et al. supports these findings, emphasizing that neuroendocrine mediators bridge psychological stress with alterations in microbiota community composition, intestinal permeability, and systemic inflammation relevant to the pathogenesis of acne (45).

Collectively, these data propose that stress is not merely a psychosocial consequence of acne but an etiologically active disease-promoting factor that perpetuates disease through mechanisms of neuroimmune and microbiome involvement(44–46) Finally, several reviews concur on the neuroendocrine–immune relationship between microbiota and acne. Lee et al. argues that C. acnes is not the sole microbial inducer of acne, as dysbiosis

Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

within creatures such as Prevotella and Malassezia also initiate inflammatory cascades, expanding the list of microbes implicated in acne(38). Zhang et al. and Borrel et al. highlight the manner in which stress hormones such as cortisol, catecholamines, and neuropeptides regulate both microbial virulence and sebocyte metabolism to form a mechanistic triad of stress, microbiota, and cutaneous inflammation (45,46). Sánchez-Pellicer et al. demonstrates that probiotics containing Lactobacillus and Bifidobacterium have the potential to restore microbial diversity, reduce systemic inflammation, and modulate lipid metabolism, suggesting microbiota-based treatments might complement conventional treatments and address physiological as well as psychosocial dimensions of acne (24,31). Collectively, these findings show that acne is not one dermatological condition but a systemic disorder resulting from the dynamic interaction between microbial dysbiosis, neuroendocrine stress responses, oxidative stress, and diet (24,31,38,45,46). Figure 2 illustrates the complex interaction between stress, diet, intestinal microbiota, and the brain–skin axis during acne pathogenesis.(38,51) From a therapeutic perspective, an integrated model of acne supports using proven therapies retinoids, antimicrobials, and hormonal therapy with the addition of adjunctive therapy including stress control, dietary change, and interventions based on the microbiome (11,13,33,48). Probiotic supplementation, prebiotics, and even new investigational techniques such as fecal microbiota transplantation are promising but uncharted directions(11,19,48,49). Psychological support, including mindfulness and cognitive-behavioral therapy, not only enhances psychologic well-being but also maximizes adherence to dermatologic regimens(15,17,21). Nevertheless, there are still major gaps. First, most studies are either observational or cross-sectional, restricting causal inference (6,15,21,28). Randomized controlled trials are very few in stress-related and probiotic interventions (12,48). Second, heterogeneity of methods—such as varying stress measurement scales, microbiome sequencing techniques, and dietary assessment instruments—hinders comparability across studies. Third, although Mendelian randomization studies identify causal microbial taxa, the greater part of the gut microbiome is uninvestigated(4,26). Lastly, psychosocial interventions, although demonstrated to enhance

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

outcomes, continue to be underused in dermatology practice because of stigma and constraints on resources (15,17,21).

Conclusion

In summary, acne vulgaris is a multifactorial etiologic disorder where stress, gut microbiota, and skin microbial dysbiosis converge to shape disease onset and severity. Integrating classic dermatologic treatment with stress-reducing treatments, dietary modifications, and microbiome-targeted therapies may be a more complete and effective treatment method for acne. Future work needs to overcome longitudinal, controlled investigations of psychological, dietary, and microbiome factors in a simultaneous manner in order to deliver personalized, evidence-based treatment programs.

REFERENCES

1. Dréno B, Dagnelie MA, Khammari A, Corvec S. The Skin Microbiome: A New Actor in Inflammatory Acne. Am J Clin Dermatol. 2020 Sep;21(S1):18–24. https://doi.org/10.1007/s40257-020-00531-1
2. Salem I, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. Front Microbiol. 2018 Jul 10;9:1459. https://doi.org/10.3389/fmicb.2018.01459
3. Zari S, Alrahmani D. The association between stress and acne among female medical students in Jeddah, Saudi Arabia. Clin Cosmet Investig Dermatol. 2017 Dec;Volume 10:503–6. https://doi.org/10.2147/CCID.S148499
4. Feng F, Li R, Tian R, Wu X, Zhang N, Nie Z. The causal relationship between gut microbiota and immune skin diseases: A bidirectional Mendelian randomization. Mentino D, editor. PLOS ONE. 2024 Mar 21;19(3):e0298443. https://doi.org/10.1371/journal.pone.0298443
5. Bouraqqadi O, Soughi M, Maiouak M, Douhi Z, Elloudi S, BayBay H, et al. The impact of academic stress on acne: An observational cohort study among medical students in

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

Morocco. JAAD Int. 2025 Feb;18:154–5. https://doi.org/10.1016/j.jdin.2024.09.019

6. Li J, Mao B, Tang X, Zhang Q, Zhao J, Zhang H, et al. Targeting the Diet–Gut–Skin Axis for Acne Amelioration: Unveiling Regulatory Mechanisms of Dietary Components and Future Perspectives. Food Rev Int. 2025 May 2;1–24. https://doi.org/10.1080/87559129.2025.2494063
7. Bhaijamal RA, Nayak SPS. The Impact of Stress on Acne. https://doi.org/10.22270/ajprd.v11i3.1272
8. Zhang H, Wang M, Zhao X, Wang Y, Chen X, Su J. Role of stress in skin diseases: A neuroendocrine-immune interaction view. Brain Behav Immun. 2024 Feb;116:286–302. https://doi.org/10.1016/j.bbi.2023.12.005
9. Panggabean HT. THE INFLUENCE OF STRESS LEVELS ON ACNE VULGARIS IN STUDENTS OF STATE ISLAMIC UNIVERSITY NORTH SUMATERA MEDAN. https://doi.org/10.32832/hearty.v13i3.19997
10. Munteanu C, Turti S, Marza SM. Unraveling the Gut–Skin Axis: The Role of Microbiota in Skin Health and Disease. Cosmetics. 2025 Aug 8;12(4):167. https://doi.org/10.3390/cosmetics12040167
11. Madejska M, Rudzka A, Drzewiecka A, Drzewiecki A, Korczak W, Gaszyńska M, et al. The influence of stress and other behavioural factors on the onset and exacerbation of acne - a review of pathogenetic mechanisms, interactions between body systems and directions for therapeutic strategies. Qual Sport. 2025 Apr 14;40:59769. https://doi.org/10.12775/QS.2025.40.59769
12. Widhiati S, Purnomosari D, Wibawa T, Soebono H. The role of gut microbiome in inflammatory skin disorders: a systematic review. Dermatol Rep. 2021 Dec 28. https://doi.org/10.4081/dr.2022.9188
13. Pai VV, Sarath AP, Kerkar Z. Gut microbiome in dermatology – A narrative review. Indian J Dermatol Venereol Leprol. 2025 Mar 4;0:1–11.

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

https://doi.org/10.25259/IJDVL_1094_2024

14. Jović A, Marinović B, Kostović K, Čeović R, Basta-Juzbašić A, Mokos ZB. The Impact of Pyschological Stress on Acne.
15. Majd M, Graham-Engeland JE, Smyth JM, Sliwinski MJ, Lipton RB, Katz MJ, et al. Distinct inflammatory response patterns are evident among men and women with higher depressive symptoms. Physiol Behav. 2018 Feb;184:108–15. https://doi.org/10.1016/j.physbeh.2017.11.009
16. Bouraqqadi O, Soughi M, Maiouak M, Douhi Z, Elloudi S, BayBay H, et al. The impact of academic stress on acne: An observational cohort study among medical students in Morocco. JAAD Int. 2025 Feb;18:154–5. https://doi.org/10.1016/j.jdin.2024.09.019
17. The correlation between academic stress, sleep quality, and acne severity: a longitudinal cohort study. Khyber Med Univ J. 2025 Jun 30. https://doi.org/10.35845/kmuj.2025.23614
18. Aziz F, Khan MF. Association of Academic Stress, Acne Symptoms and Other Physical Symptoms in Medical Students of King Khalid University. Int J Environ Res Public Health. 2022 Jul 18;19(14):8725. https://doi.org/10.3390/ijerph19148725
19. Yosipovitch G, Tang M, Dawn A, Chen M, Goh C, Huak Y, et al. Study of Psychological Stress, Sebum Production and Acne Vulgaris in Adolescents. Acta Derm Venereol. 2007;87(2):135–9. https://doi.org/10.2340/00015555-0231
20. Jusuf NK, Putra IB, Sutrisno AR. Correlation Between Stress Scale and Serum Substance P Level in Acne Vulgaris. Int J Gen Med. 2021 Mar;Volume 14:681–6. https://doi.org/10.2147/IJGM.S294509
21. Kiu LY. The Gut-brain-skin Axis and Acne Vulgaris: Current Understanding and the Management Implications. Clin Dermatol Rev. 2025 Jul;9(3):213–9. https://doi.org/10.4103/cdr.cdr_102_22
22. Barankin B, DeKoven J. Psychosocial effect of common skin diseases.

DOI: http://doi.org/10.5281/zenodo.20813676

https://pubmed.ncbi.nlm.nih.gov/12046366/

23. Sánchez-Pellicer P, Navarro-Moratalla L, Núñez-Delegido E, Ruzafa-Costas B, Agüera-Santos J, Navarro-López V. Acne, Microbiome, and Probiotics: The Gut–Skin Axis. Microorganisms. 2022 Jun 27;10(7):1303. https://doi.org/10.1016/j.microb.2025.100342
24. Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut Pathog. 2011;3(1):1. https://doi.org/10.1186/1757-4749-3-1
25. Bataille V, Snieder H, MacGregor AJ, Sasieni P, Spector TD. The Influence of Genetics and Environmental Factors in the Pathogenesis of Acne: A Twin Study of Acne in Women. J Invest Dermatol. 2002 Dec;119(6):1317–22. https://doi.org/10.1046/j.1523-1747.2002.19621.x
26. Vasam M, Korutla S, Bohara RA. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. Biochem Biophys Rep. 2023 Dec;36:101578. https://doi.org/10.1016/j.bbrep.2023.101578
27. Cao Q, Guo J, Chang S, Huang Z, Luo Q. Gut microbiota and acne: A Mendelian randomization study. Skin Res Technol. 2023 Sep;29(9):e13473.
28. He X, Zhang Z, Jiang H, Luo H, Gan Q, Wei K, et al. Causal association of gut microbes and blood metabolites with acne identified through systematic mendelian randomization. Sci Rep. 2024 Nov 5;14(1):26816. https://doi.org/10.1038/s41598-024-78603-z
29. Ji X, Wu S, Zhao D, Bai Q, Wang Y, Gong K, et al. Revealing the Impact of Gut Microbiota on Acne Through Mendelian Randomization Analysis. Clin Cosmet Investig Dermatol. 2024 Feb;Volume 17:383–93. https://doi.org/10.2147/CCID.S451104
30. Sanchez-Lopez MF, Barrero-Caicedo PA, Olmos-Carval HM, Torres-Medina AF, Alzate-Granados JP. Relationship between skin and gut microbiota dysbiosis and inflammatory skin diseases in adult patients: A systematic review. The Microbe. 2025 Jun;7:100342. https://doi.org/10.1016/j.microb.2025.100342

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

31. Huang Y, Liu L, Hao Z, Chen L, Yang Q, Xiong X, et al. Potential roles of gut microbial tryptophan metabolites in the complex pathogenesis of acne vulgaris. Front Microbiol. 2022 Jul 27;13:942027. https://doi.org/10.3389/fmicb.2022.942027
32. Mahmud MdR, Akter S, Tamanna SK, Mazumder L, Esti IZ, Banerjee S, et al. Impact of gut microbiome on skin health: gut-skin axis observed through the lenses of therapeutics and skin diseases. Gut Microbes. 2022 Dec 31;14(1):2096995. https://doi.org/10.1080/19490976.2022.2096995
33. Ni Q, Zhang P, Li Q, Han Z. Oxidative Stress and Gut Microbiome in Inflammatory Skin Diseases. Front Cell Dev Biol. 2022 Mar 7;10:849985. https://doi.org/10.3389/fcell.2022.849985
34. Bungau AF, Radu AF, Bungau SG, Vesa CM, Tit DM, Endres LM. Oxidative stress and metabolic syndrome in acne vulgaris: Pathogenetic connections and potential role of dietary supplements and phytochemicals. Biomed Pharmacother. 2023 Aug;164:115003. https://doi.org/10.1016/j.biopha.2023.115003
35. Baldwin H, Tan J. Effects of Diet on Acne and Its Response to Treatment. Am J Clin Dermatol. 2021 Jan;22(1):55–65. https://doi.org/10.1007/s40257-020-00542-y
36. Cunliffe WJ, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. Br Med J. 2025.
37. Lee YB, Byun EJ, Kim HS. Potential Role of the Microbiome in Acne: A Comprehensive Review. J Clin Med. 2019 Jul 7;8(7):987. https://doi.org/10.3390/jcm8070987
38. Alzahrani LA, Alfurayh NA, Jadaan NS, Alqahtani RS, Alqahtani BA. Impact of Stress on the Prevalence of Acne Among Medical Students in the Middle East: A Systematic Review. Cureus. 2025 Aug 23. https://doi.org/10.7759/cureus.90815
39. Basfar AS, Jawhari AM, Alotaibi MN, Alzahrani ES, Aseeri IA, Atalla AA. Severity of acne, stress, and food habits of medical students at Taif University, Saudi Arabia. J Fam Community Med. 2023 Apr;30(2):131–6https://doi.org/10.4103/jfcm.jfcm_396_22

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

Haya et al - 2026

DOI: http://doi.org/10.5281/zenodo.20813676

40. Nagamine T. Gut-skin-brain axis in people suffering from sepsis with acute skin failure. World J Psychiatry. 2025 Jul 19;15(7). https://doi.org/10.5498/wjp.v15.i7.106062
41. Maiuolo J, Gliozzi M, Musolino V, Carresi C, Scarano F, Nucera S, et al. The Contribution of Gut Microbiota–Brain Axis in the Development of Brain Disorders. Front Neurosci. 2021 Mar 23;15:616883. https://doi.org/10.3389/fnins.2021.616883
42. Arican O, Kurutas EB, Sasmaz S. Oxidative Stress in Patients With Acne Vulgaris. Mediators Inflamm. 2005 Jan;2005(6):380–4. https://doi.org/10.1155/MI.2005.380
43. Jusuf NK, Putra IB, Sutrisno AR. Correlation Between Stress Scale and Serum Substance P Level in Acne Vulgaris. Int J Gen Med. 2021 Mar;Volume 14:681–6. https://doi.org/10.2147/IJGM.S294509
44. Borrel V, Thomas P, Catovic C, Racine PJ, Konto-Ghiorghi Y, Lefeuvre L, et al. Acne and Stress: Impact of Catecholamines on Cutibacterium acnes. Front Med. 2019 Jul 10;6:155. https://doi.org/10.3389/fmed.2019.00155
45. Zhang H, Wang M, Zhao X, Wang Y, Chen X, Su J. Role of stress in skin diseases: A neuroendocrine-immune interaction view. Brain Behav Immun. 2024 Feb;116:286–302. https://doi.org/10.1016/j.bbi.2023.12.005
46. Instytut Zdrowia Publicznego, Katedra Epidemiologii i Badań Populacyjnych, Uniwersytet Jagielloński Collegium Medicum, Gradowicz-Prajsnar B. Stress and skin diseases. Overview using acne vulgaris as an example. Aesthetic Cosmetol Med. 2023 Dec;12(6):207–12. https://doi.org/10.52336/acm.2023.027
47. Author N, Widiyanti D, Arsyad M. The Effect Of Learning Stress In The Faculty Of Medicine On The Arising Of Acne Vulgaris In Students Of The Faculty Of Medicine YARSI University And Its Review From The Islamic View. Jr Med J. 2023 Jun 4;1(5):581–9.https://doi.org/10.4081/dr.2022.9188
48. Chilicka K, Dzieńdziora-Urbińska I, Szyguła R, Asanova B, Nowicka D. Microbiome and Probiotics in Acne Vulgaris—A Narrative Review. Life. 2022 Mar 15;12(3):422.

DOI: http://doi.org/10.5281/zenodo.20813676

https://doi.org/10.3390/life12030422

49. Sivamani RK, Maloh J, Nong Y. Correlating the Gut Microbiota and Circulating Hormones with Acne Lesion Counts and Skin Biophysical Features. Microorganisms. 2023 Aug 9;11(8):2049. https://doi.org/10.3390/microorganisms11082049
50. A D, J M. 34684 Diet and quality of life in acne: A gut-brain-skin axis approach. J Am Acad Dermatol. 2022 Sep;87(3):AB43. https://doi.org/10.1016/j.jaad.2022.06.204
51. Munteanu C, Turti S, Marza SM. Unraveling the Gut–Skin Axis: The Role of Microbiota in Skin Health and Disease. Cosmetics. 2025 Aug 8;12(4):167. https://doi.org/10.3390/cosmetics12040167